*REMARKS*

*Office Action*

The Office has withdrawn from consideration claims 1-46 as non-elected claims. Groups I (claims 1-19) and III (claims 39, 41, 43 and 44) have been rejoined. Groups II (claims 20-38) and IV (claims 40, 42 and 45) have been rejoined. Groups VI (claims 47-62) and VII (claims 63 and 64) have been rejoined.

The Office alleges that the oath or declaration is defective.

The Office further alleges that the Information Disclosure Statement ("IDS") does not comply with 37 C.F.R. § 1.98.

Claims 63-66 have been objected to as allegedly being in improper form.

Claims 47 and 49-66 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

Reconsideration of the objections and rejections is requested.

*Amendments to the Claims*

Claims 1-46 have been canceled, without prejudice, as being directed to non-elected subject matter. Applicants reserve the right to pursue the subject matter of any of claims 1-46 in a continuing application, e.g., a divisional.

Claim 63 has been amended to read as an independent claim by replacing the reference to claim 47 with the structural definition recited therein. New claims 67 and 78 more particularly recite mutant retroviruses. New claims 68-77 recite preferred compounds for practicing the claimed method.

The foregoing amendments are fully supported by the specification, e.g., from p. 33, line 19, to p. 37, line 25; from p. 45, line 1, to p. 50, line 17; p. 81 (Table 4); p. 84, line 1, to p. 93, line 19; and claims 47-59 of the specification as originally filed. No new matter has been added thereby.

*Oath/Declaration*

The Office alleges that the oath or declaration lacks information concerning the signature, country of citizenship, residence and postal address for the inventor Hiroaki Mitsuya. Contrary to the Office's assertion, Applicants' records indicate that the signature, country of citizenship, residence and postal address for Hiroaki Mitsuya, in fact, all appear on the last page (p. 4) of the Combined Declaration and Power of Attorney, filed on March 7,

2001. Attached herewith are copies of the Combined Declaration and Power of Attorney, which includes the required information for Hiroaki Mitsuya, and the return postcard bearing a stamp in which the Office has acknowledged receipt of the same.

In view of the foregoing, it is evident that the Combined Declaration and Power of Attorney is not defective as alleged. As such, Applicants should not be required to submit a new oath or declaration as required by the Office Action, and the Office is respectfully requested to acknowledge acceptance of the Combined Declaration and Power of Attorney as originally filed.

*Information Disclosure Statement*

The Office Action asserts that the IDS filed on "05/26/01" does comply not with 37 C.F.R. § 1.98(a)(2) on the grounds that Applicants allegedly did not provide copies of some of the non-patent literature and foreign patent documents. The Office Action additionally asserts that the reference WO 90/09191 does not include a concise statement of relevance.

Contrary to the Office Action, our records indicate that on March 23, 2001, the IDS was in fact filed along with copies of all of the cited references (AA-BX), receipt of which was acknowledged by the Office. Attached herewith are copies of the original IDS (including the original Form PTO-1449) and the return postcard bearing a stamp acknowledging the Office's receipt of the IDS and references AA-BX. Also attached for the Examiner's convenience are copies of the references that the Office alleges were not provided with the IDS originally. It should be noted further that the front page of WO 90/09191 includes an English-language abstract, which may be submitted in lieu of a concise statement of relevance under 37 C.F.R. § 1.98(b).

In view of the foregoing, it is evident that the IDS and cited references all have been filed and received by the Office. As such, the Office is respectfully requested to fully consider *all* of the cited references and to indicate that full consideration has been given by returning to Applicants a properly executed Form PTO-1449 bearing the Examiner's initials in the spaces adjacent to the citations for references AJ, AK, AQ through AT, AV through BG, BI through BK, and BM through BX.

*Discussion of Claim Objections*

Claim 63 has been re-written to read as an independent claim, as suggested by the Examiner. The amendment of claim 63 is believed to render moot the objections to claims 63-66.

*Discussion of the Enablement Rejection*

In support of the enablement rejection, the Office Action contends that the present specification would not have taught one of skill in the art how to make and/or use the claimed invention without undue experimentation. Contrary to the Office Action, the specification as originally filed teaches one of the ordinary skill in the art how to practice the full scope of the claimed method without undue experimentation.

The specification teaches how to prepare, characterize, and biologically test the recited compounds. For example, the specification, e.g., from p. 33, line 19, to p. 50, line 17, and Figs. 3A, 3B, 5A-5D, teaches the molecular structures of the recited compounds, which are useful for practicing the claimed method. In addition, the specification, e.g., from p. 61, line 10, to p. 73, line 25, and Figs. 1-4, teaches methods for synthetically preparing, isolating and characterizing the recited compounds. Further, the specification, e.g., from p. 12, line 2, to p. 33, line 18, and from p. 74, line 1, to p. 76, line 16, teaches assay methods for biologically testing the recited compounds.

The specification teaches methods of formulating and therapeutically administering the recited compounds. For example, the specification, e.g., from p. 50, line 18, to p. 56, line 31, teaches methods of formulating therapeutically effective amounts of the recited compounds to produce pharmaceutical compositions, e.g., for oral, injectable, rectal, topical and pulmonary administration. In addition, the specification, e.g., from p. 57, line 1, to p. 60, line 9, further teaches therapeutically effective dosages and therapeutic methods of administering the recited compounds and compositions.

The specification further provides data, which demonstrate the biological efficacy of the recited compounds. The specification, e.g., from p. 76, line 18, to p. 79, line 22, and from p. 84, line 22, to p. 93, line 20, provides data demonstrating the potent, broad spectrum antiviral activity of exemplary compounds against a panel of multiply mutated, multi-drug resistant HIV isolated from HIV-infected humans. The specification, e.g., from p. 84, lines 1-20, further provides data demonstrating the potent inhibitory activity of exemplary compounds against HIV proteases that contain deleterious mutations associated with drug resistance.

Moreover, the specification at, e.g., p. 82, lines 4-23, provides *in vivo* data demonstrating the high blood levels achieved by oral administration of an exemplary compound useful for practicing the claimed method. The specification at, e.g., p. 83, lines 5-27, still further provides data demonstrating that high potency can be maintained even in the presence of excessive amounts of human binding proteins, which are believed to adversely impact *in vivo* efficacy. As such, the specification as originally filed provides abundant

guidance and direction, and clearly teaches one of ordinary skill how to practice the full scope of the claimed method.

Contrary to the Office Action, any experimentation that may be necessary is not "undue." The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *See* MPEP § 2164.01. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *Id.* In the instant case, the specification teaches methods for synthesizing the active compounds using reagents and preparative techniques, which were well known in the art of organic chemistry at the time that the present application was filed. Further, methods of formulating and administering the recited compounds can be performed using materials and methods, which were well known in the pharmaceutical arts at the time that the present application was filed. This is made abundantly clear by the present specification e.g., at p. 59, lines 7-17, which states:

> One skilled in the art will recognize that the specific dosage level for any particular patient will depend upon a variety of factors including, for example, the activity of the specific compound employed, the age, body weight, general health, sex, diet, time of administration, route of administration, rate of excretion, drug combination, CD4 count, the potency of the active compound with respect to the particular mutant retroviral strain to be inhibited, and the severity of the symptoms presented prior to or during the course of therapy.

As such, the specification teaches utilizing the type of development work that the pharmaceutical arts routinely engage in, and not "undue" experimentation.

The Office Action (p. 8) further contends that the examples are not enabling "because most of the examples are directed to an *in vitro* use ... with the exception of one example." In this regard, the Office Action (p. 8) asserts that Applicants' *in vivo* data "lacks correlation or data that connects the claimed invention with the oral absorption data." Contrary to the Office's assertion, the specification provides an abundance of data demonstrating that the recited compounds should be effective for practicing the claimed method.

The fact that HIV may ultimately be capable of developing resistance to virtually any anti-HIV agent does not render Applicants' invention inoperable, since the claimed methods do not require absolute preclusion of resistance. In this regard, it is important to point out that the term "prevent" itself is not necessarily absolute. This is made clear by the definitions

ascribed to "prevent," which include: "To keep from happening. ... To keep (someone) from doing something; impede. ... To anticipate or counter in advance. ... To come before; precede. ... To present an obstacle." (*The American Heritage® College Dictionary*, Third Ed.). As such, it is clear that prevention, by definition, need not be absolute, and particularly within the context of anti-HIV drug therapy.

The attached Declaration has been submitted as further evidence to show that there is indeed a reasonable correlation between the data provided by Applicants' specification and the claimed method. In this regard, the attached Declaration shows that Applicants' specification supports a reasonable expectation that the claimed method will be therapeutically effective *in vivo*. The attached Declaration further shows that a recited compound for practicing the claimed method is *in fact* orally efficacious in humans for treating multi-drug resistant HIV infection.

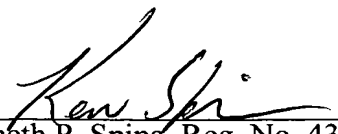
Moreover, the MPEP states: "If reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process." *See* MPEP § 2107.03. The present specification amply provides such correlative data. Thus, it is clear that one need only look to the specification to determine that the claimed method is, in fact, fully enabled.

In view of the foregoing, the specification is fully enabling for the entire scope of the subject matter recited in the pending claims. Accordingly, the rejections of claims 47 and 49-66 should be withdrawn.

*Conclusion*

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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